

53. (New) The process of claim 51 wherein said step (g) is conducted prior to step (e) for the addition of at least one monomeric subunit to each of said oligomeric compounds..

54. (New) The process of claim 51 wherein said step (g) is conducted prior to each iteration of said step (e).

55. (New) The process of claim 51 wherein said step (g) is conducted only after at least one iteration of said step (e).

56. (New) The process of claim 51 wherein said step (g) is conducted after said step (f) for the addition of at least one monomeric subunit to each of said oligomeric compounds.

#### **REMARKS**

After entry of the proposed amendment, claims 31-56 will be pending in this application. Claims 2-8, 1-14, 16-20, 22-26, and 27-30 have been canceled and rewritten as new claims 31-56. Prior independent claim 27 corresponds to new claim 31; prior independent claim 28 corresponds to new claim 39; prior independent claim 29 corresponds to new claim 45; and prior independent claim 30 corresponds to new claim 51. No new matter has been added.

The Office Action includes rejections under 35 U.S.C. §§ 103(a), 112, second paragraph, and under the judicially created doctrine of obviousness-type double patenting. In view of the remarks to follow, Applicants request that these rejections be reconsidered and withdrawn.

**Rejections Under 35 U.S.C. § 112, ¶2**

Claims 1-26 stand rejected under 35 U.S.C. 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the foregoing amendments, however, Applicants respectfully submit that this rejection is now moot.

**Obvious-Type Double Patenting**

Claims 16-20, 22-26, 29 and 30 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 23 and 24 of commonly owned U.S. Patent No. 5,714,606 to Acevedo, in view of either of Letsinger et al. (U.S. Patent No. 5,112,962) or Smith et al. (U.S. Patent No. 5,015,733). Applicants respectfully request reconsideration of this rejection in view of the foregoing amendments.

In particular, prior claims 29 and 30 (new claims 45 and 51, respectively) have been amended to recite the phrase "provided that at least one of said aminodiol monomer subunits in each oligomeric compound of said library does not have structure III." Support for this amendment can be found in Applicants' specification at, for example, page 8, lines 26-28. Applicants respectfully submit that this amendment circumvents the Acevedo patent. Accordingly, Applicants believe that this rejection is now moot.

In any event, should the Examiner determine that the double patenting rejection still applies, Applicants request that the rejection be deferred pending some identification of allowable subject matter, as it likely can be readily resolved (depending upon the subject matter ultimately allowed) through the filing of a suitable terminal disclaimer.

**Rejections Under 35 U.S.C. § 103(a)**

Claims 16-20, 22-26, 29 and 30 have been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 5,714,606 to Acevedo ("the Acevedo patent"), in view of either of Letsinger et al. (U.S. Patent No. 5,112,962) ("the Letsinger patent") or Smith et al. (U.S. Patent No. 5,015,733) ("the Smith patent"). Applicants respectfully request reconsideration of this rejection in view of the foregoing amendments.

In particular, prior claim 30 (new claim 51), for example, has been amended to recite the phrase "provided that at least one of said aminodiol monomer subunits in each oligomeric compound of said library does not have structure III." Support for this amendment can be found in Applicants' specification at, for example, page 8, lines 26-28. A similar limitation has been added to prior claim 29 (new claim 45). Applicants respectfully assert that the presently claimed subject matter is not obvious in view of the Acevedo patent, which does not disclose or suggest oligomers having any of structures I, II, III, IV, V, or VI. Accordingly, Applicants respectfully request withdrawal of the rejection.

DOCKET NO.: ISIS-2297



PATENT

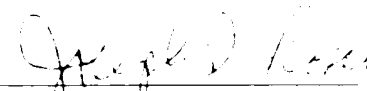
**Conclusion**

Applicant believes that the present claims are now in condition for allowance.

An early Office Action to that effect is, therefore, earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Respectfully submitted,

  
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DOCKET NO.: ISIS-2297

PATENT

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend the application as follows:

**In the Specification:**

At page 1, line 1 of the specification, please delete the Title and replace it with the following new Title: **--OLIGOMERIC COMPOUNDS AND LIBRARIES OF SUCH COMPOUNDS COMPRISING A PLURALITY OF AMINODIOL MONOMER SUBUNITS--.**

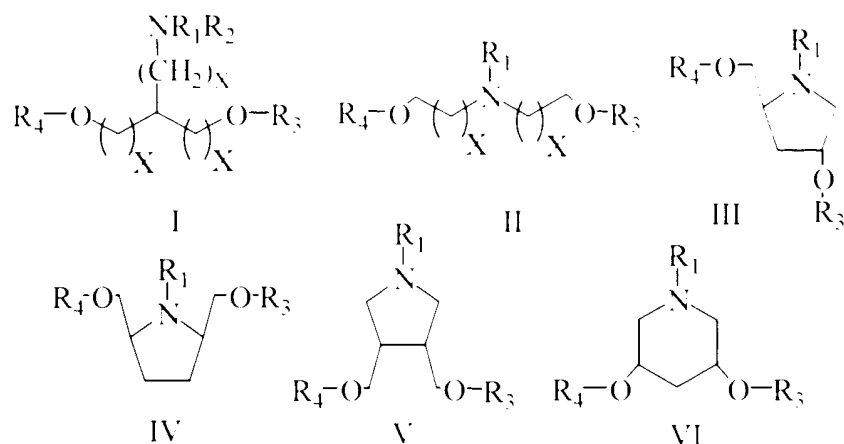
At page 1, replace the paragraph beginning on line 3 with the following replacement paragraph:

--This application is a continuation-in-part of United States Application Serial No. 08/483,311, filed 6/7/95[:], now U.S. Patent No. 6,184,389, which is a continuation-in-part of PCT application Serial No. PCT/US95 /00356 filed 1/11/95, which is a continuation-in-part of United States Application Serial No. 08/180,134, filed 1/11/94[:], which is a continuation in part of United States Application 08/179,970, filed 1/11/94 which issued on 5/21/96 as U.S. Patent Serial No. 5519134. Each of these patent applications are assigned to the assignee of this application and are incorporated by reference herein.

**In the claims:**

Please cancel claims 2-8, 10-14 16-20, 22-26, and 27-30, without prejudice, and replace them with new claims 31-56:

--31. (New) An oligomeric compound comprising a plurality of aminodiol monomer subunits joined by linking groups, wherein each of said aminodiol monomer subunits has one of the structures I, II, III, IV, V or VI:



wherein:

each x is, independently, 0 to 5;

$R_1$  is -T-L or a base labile protecting group;

T is a single bond, a methylene group or a group having formula:



wherein:

$R_{10}$  is =O, =S, or =NR<sub>11</sub>;

$R_5$  and E, independently, are a single bond, CH=CH, C≡C, O, S, NR<sub>11</sub>, or C<sub>6</sub>-C<sub>14</sub> aryl;

each  $R_6$ ,  $R_7$ ,  $R_8$ ,  $R_9$ ,  $R_{11}$ ,  $R_{12}$  and  $R_{13}$  are, independently, H, alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, or aryl having 7 to about 14 carbon atoms;

m and n, independently, are 0 to 5;

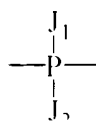
p is 0 or 1;

q is 1 to about 10;

L is H, substituted or unsubstituted  $C_2-C_{10}$  alkyl, substituted or unsubstituted  $C_2-C_{10}$  alkenyl, substituted or unsubstituted  $C_2-C_{10}$  alkynyl, substituted or unsubstituted  $C_4-C_{10}$  carbocyclic alkyl, substituted or unsubstituted  $C_4-C_{10}$  carbocyclic alkenyl, substituted or unsubstituted  $C_4-C_{10}$  carbocyclic alkynyl, substituted or unsubstituted  $C_6-C_{14}$  aryl, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, a nitrogen containing heterocycle, a sulfur containing heterocycle, an oxygen containing heterocycle, a metal coordination group, a conjugate group, halogen, hydroxyl (OH), thiol (SH), keto (C=O), carboxyl (COOH), amide (CONR<sub>12</sub>), amidine (C(=NH)NR<sub>12</sub>R<sub>13</sub>), guanidine (NHC(=NH)NR<sub>12</sub>R<sub>13</sub>), glutamyl (R<sub>12</sub>OOCCH(NR<sub>12</sub>R<sub>13</sub>)(CH<sub>2</sub>)<sub>2</sub>C(=O)), nitrate (ONO<sub>2</sub>), nitro (NO<sub>2</sub>), nitrile (CN), trifluoromethyl (CF<sub>3</sub>), trifluoromethoxy (OCF<sub>3</sub>), O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, amino (NH<sub>2</sub>), azido (N<sub>3</sub>), hydrazino (NHNH<sub>2</sub>), hydroxylamino (ONH<sub>2</sub>), sulfoxide (SO), sulfone (SO<sub>2</sub>), sulfide (S-), disulfide (S-S), silyl, a nucleosidic base, an amino acid side chain, a carbohydrate, a biopharmaceutically active moiety, or group capable of hydrogen bonding where the substituent groups are selected from hydroxyl, amino, alkoxy, alcohol, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, and alkynyl groups:

R<sub>2</sub> is hydrogen or C<sub>1</sub>-C<sub>10</sub> alkyl:

R<sub>3</sub> and R<sub>4</sub> are independently hydrogen, an acid labile hydroxyl protecting group, a linking group or a conjugate group, wherein said linking group has the formula:



wherein:

$J_1$  is =O or =S;

$J_2$  is OH or  $N(Y_n)T_n$ ;

$Y_n$  is H or  $(Q_2)_j-Z_2$ ;

$T_n$  is  $(Q_1)_k-Z_1$ , or together  $Y_n$  and  $T_n$  are joined in a nitrogen heterocycle;

$Q_1$  and  $Q_2$  independently are  $C_2-C_{10}$  alkyl,  $C_2-C_{10}$  alkenyl,  $C_2-C_{10}$  alkynyl,  $C_4-C$ -carbocyclo alkyl,  $C_4-C$ -carbocyclo alkenyl, a heterocycle, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, a polyalkyl glycol, or  $C-C_{14}$  aralkyl;

$j$  and  $k$  independently are 0 or 1;

$Z_1$  and  $Z_2$  independently are H,  $C_1-C_2$  alkyl,  $C_2-C_{20}$  alkenyl,  $C_2-C_{20}$  alkynyl,  $C_6-C_{14}$  aryl,  $C-C_{15}$  aralkyl, halogen,  $CH=O$ ,  $OR_{12}$ ,  $SR_{12}$ ,  $NR_{12}R_{13}$ ,  $C(=NH)NR_{12}R_{13}$ ,  $CH(NR_{12}R_{13})$ ,  $NHC(=NH)NR_{12}R_{13}$ ,  $CH(NH_2)C(=O)OH$ ,  $C(=O)NR_{12}R_{13}$ ,  $C(=O)OR_{12}$ , a metal coordination group, a reporter group, a nitrogen-containing heterocycle, a purine, a pyrimidine, a phosphate group, a polyether group, or a polyethylene glycol group; and

provided that at least one of said aminodiols monomer subunits in said oligomeric compound does not have structure III.

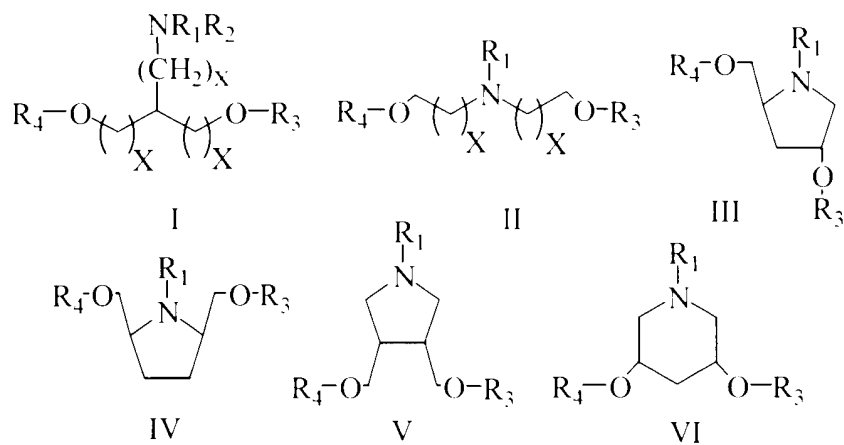
32. (New) The oligomeric compound of claim 31 wherein said  $J_1$  is =O or =S and said  $J_2$  is OH.

33. (New) The oligomeric compound of claim 31 wherein said  $J_1$  is =O, said  $J_2$  is  $N(Y_n)T_n$  and at least two of said  $N(Y_n)T_n$  are the same.

34. (New) The oligomeric compound of claim 31 wherein said  $J_1$  is =O, said  $J_2$  is  $N(Y_n)T_n$  and wherein at least two of said  $N(Y_n)T_n$  are different.



35. (New) The oligomeric compound of claim 31 wherein each of said  $R_i$  are the same.
36. (New) The oligomeric compound of claim 31 wherein at least two of said  $R_i$  are different.
37. (New) The oligomeric compound of claim 31 wherein each of said aminodiol monomer subunits are the same.
38. (New) The oligomeric compound of claim 31 wherein at least two of said aminodiol monomer subunits are different.
39. (New) A library of oligomers, each of said oligomers comprising a plurality of aminodiol monomer subunits joined by linking groups, said aminodiol monomer subunits, each of said subunits having structure I, II, III, IV, V or VI:



wherein:

each  $x$  is, independently, 0 to 5;

$R_i$  is -T-L or a base labile protecting group;

T is a single bond, a methylene group or a group having formula:



wherein:

$R_{10}$  is =O, =S, or =NR<sub>11</sub>;

$R_8$  and E, independently, are a single bond, CH=CH, C≡C, O, S, NR<sub>11</sub>, or C<sub>n</sub>-C<sub>14</sub> aryl;

each  $R_6$ ,  $R_7$ ,  $R_8$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  and  $R_{13}$  are, independently, H, alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, or aryl having 7 to about 14 carbon atoms;

m and n, independently, are 0 to 5;

p is 0 or 1;

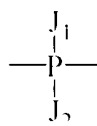
q is 1 to about 10;

L is H, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkynyl, substituted or unsubstituted C<sub>4</sub>-C- carbocyclic alkyl, substituted or unsubstituted C<sub>4</sub>-C- carbocyclic alkenyl, substituted or unsubstituted C<sub>4</sub>-C- carbocyclic alkynyl, substituted or unsubstituted C<sub>6</sub>-C<sub>14</sub> aryl, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, a nitrogen containing heterocycle, a sulfur containing heterocycle, an oxygen containing heterocycle, a metal coordination group, a conjugate group, halogen, hydroxyl (OH), thiol (SH), keto (C=O), carboxyl (COOH), amide (CONR<sub>12</sub>), amidine (C(=NH)NR<sub>12</sub>R<sub>13</sub>), guanidine (NHC(=NH)NR<sub>12</sub>R<sub>13</sub>), glutamyl (R<sub>12</sub>OOCCH(NR<sub>12</sub>R<sub>13</sub>)(CH<sub>2</sub>)<sub>2</sub>C(=O)), nitrate (ONO<sub>2</sub>), nitro (NO<sub>2</sub>), nitrile (CN), trifluoromethyl (CF<sub>3</sub>), trifluoromethoxy (OCF<sub>3</sub>), O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, amino (NH<sub>2</sub>), azido (N<sub>3</sub>), hydrazino (NHNH<sub>2</sub>), hydroxylamino (ONH<sub>2</sub>), sulfoxide (SO), sulfone (SO<sub>2</sub>), sulfide (S-), disulfide (S-S), silyl, a

nucleosidic base, an amino acid side chain, a carbohydrate, a biopharmaceutically active moiety, or group capable of hydrogen bonding where the substituent groups are selected from hydroxyl, amino, alkoxy, alcohol, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, and alkynyl groups:

$R_2$  is hydrogen or  $C_1$ - $C_{10}$  alkyl;

$R_3$  and  $R_4$  are independently hydrogen, an acid labile hydroxyl protecting group, a linking group or a conjugate group, wherein said linking group has the formula:



wherein:

$J_1$  is =O or =S;

$J_2$  is OH or  $N(Y_0)T_0$ ;

$Y_0$  is H or  $(Q_2)_j-Z_2$ ;

$T_0$  is  $(Q_1)_k-Z_1$ , or together  $Y_0$  and  $T_0$  are joined in a nitrogen heterocycle;

$Q_1$  and  $Q_2$  independently are  $C_2$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{10}$  alkynyl,  $C_4$ - $C_{10}$  carbocyclo alkyl,  $C_4$ - $C_{10}$  carbocyclo alkenyl, a heterocycle, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, a polyalkyl glycol, or  $C$ - $C_{14}$  aralkyl;

$j$  and  $k$  independently are 0 or 1;

$Z_1$  and  $Z_2$  independently are H,  $C_1$ - $C_2$  alkyl,  $C_2$ - $C_{20}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl,  $C$ - $C_{18}$  aralkyl, halogen,  $CH=O$ ,  $OR_{12}$ ,  $SR_{12}$ ,  $NR_{12}R_{13}$ ,  $C(=NH)NR_{12}R_{13}$ ,  $CH(NR_{12}R_{13})$ ,  $NHC(=NH)NR_{12}R_{13}$ ,  $CH(NH_2)C(=O)OH$ ,  $C(=O)NR_{12}R_{13}$ ,  $C(=O)OR_{12}$ , a metal coordination group, a

reporter group, a nitrogen-containing heterocycle, a purine, a pyrimidine, a phosphate group, a polyether group, or a polyethylene glycol group; and

provided that at least one of said aminodiol monomer subunits in each oligomeric compound of said library does not have structure III.

40. (New) The library of claim 39 wherein said  $J_1$  is =O or =S and said  $J_2$  is OH.

41. (New) The library of claim 39 wherein said  $J_1$  is =O, said  $J_2$  is  $N(Y_0)T_0$  and at least two of said  $N(Y_0)T_0$  are the same.

42. (New) The library of claim 39 wherein said  $J_1$  is =O, said  $J_2$  is  $N(Y_0)T_0$  and at least two of said  $N(Y_0)T_0$  are different.

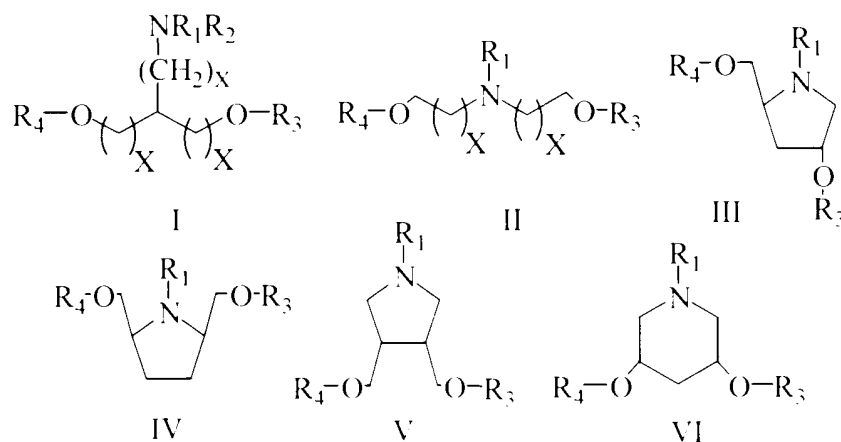
43. (New) The library of claim 39 wherein each of said  $R_1$  is the same.

44. (New) The library of claim 39 wherein at least two of said  $R_1$  are different.

45. (New) A method for preparing an oligomer comprising:

(a) selecting an aminodiol monomer subunit having the structure I, II, III, IV, V, or

VI:



wherein:

each x is, independently, 0 to 5;

$R_1$  is a base labile amino protecting group;

$R_2$  is hydrogen or  $C_1$ - $C_{10}$  alkyl;

one of  $R_3$  or  $R_4$  is hydrogen or an activated phosphite group and the other of  $R_3$  or  $R_4$  is an acid labile hydroxyl protecting group;

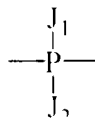
(b) attaching said aminodiol monomer subunit to a solid support to form a solid support bound aminodiol monomer subunit;

(c) treating said acid labile hydroxyl protecting group with a dilute acid to form a free hydroxyl group;

(d) reacting said free hydroxyl group with a further aminodiol monomer subunit having structure I, II, III, IV, V, or VI thereby forming an oligomeric compound bound to said solid support, said oligomeric compound containing a phosphite linkage;

(e) optionally iteratively repeating steps (c) and (d) to increase the length of the oligomeric compound bound to said solid support;

(f) optionally, prior to step (c) or after step (d) oxidizing said phosphite linkage to form a phosphate linking group wherein said linking groups are selected having formula:



wherein:

$J_1$  is =O or =S;

$J_2$  is OH or  $N(Y_1)T_1$ ;

$Y_1$  is H or  $(Q_2)_1-Z_2$ ;

$T_1$  is  $(Q_1)_k-Z_1$ , or together  $Y_1$  and  $T_1$  are joined in a nitrogen heterocycle;

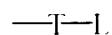
$Q_1$  and  $Q_2$  independently are  $C_2-C_{10}$  alkyl,  $C_2-C_{10}$  alkenyl,  $C_2-C_{10}$  alkynyl,  $C_4-C$ -carbocyclo alkyl,  $C_4-C$ -carbocyclo alkenyl, a heterocycle, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, a polyalkyl glycol, or  $C-C_{14}$  aralkyl;

$j$  and  $k$  independently are 0 or 1;

$Z_1$  and  $Z_2$  independently are H,  $C_1-C_3$  alkyl,  $C_2-C_{20}$  alkenyl,  $C_2-C_{20}$  alkynyl,  $C_6-C_{14}$  aryl,  $C-C_{15}$  aralkyl, halogen,  $CH=O$ ,  $OR_{12}$ ,  $SR_{12}$ ,  $NR_{12}R_{13}$ ,  $C(=NH)NR_{12}R_{13}$ ,  $CH(NR_{12}R_{13})$ ,  $NHC(=NH)NR_{12}R_{13}$ ,  $CH(NH_2)C(=O)OH$ ,  $C(=O)NR_{12}R_{13}$ ,  $C(=O)OR_{12}$ , a metal coordination group, a reporter group, a nitrogen-containing heterocycle, a purine, a pyrimidine, a phosphate group, a polyether group, or a polyethylene glycol group,

provided that at least one of said aminodiol monomer subunits in said oligomeric compound does not have structure III:

(g) prior to step (e) or after step (f) contacting said solid support bound aminodiol monomer subunit or said support bound oligomeric compound with a base to remove said base labile amino protecting group to form the solid support bound aminodiol monomer subunit or support bound oligomeric compound having a free amine, and derivatizing said free amine with a group of the formula:



wherein:

T is a single bond, a methylene group or a group having formula:



where:

$R_{10}$  is =O, =S, or =NR<sub>11</sub>;

$R_8$  and E, independently, are a single bond, CH=CH, C-C, O, S, NR<sub>11</sub>, or C<sub>6</sub>-C<sub>14</sub> aryl;

each  $R_6$ ,  $R_7$ ,  $R_8$ ,  $R_9$ ,  $R_{11}$ ,  $R_{12}$  and  $R_{13}$  are, independently, H, alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, or aryl having 7 to about 14 carbon atoms;

m and n, independently, are 0 to 5;

p is 0 or 1;

q is 1 to about 10;

L is H, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkynyl, substituted or unsubstituted C<sub>4</sub>-C- carbocyclic alkyl, substituted or unsubstituted C<sub>4</sub>-C- carbocyclic alkenyl, substituted or unsubstituted C<sub>4</sub>-C- carbocyclic alkynyl, substituted or unsubstituted C<sub>6</sub>-C<sub>14</sub> aryl, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, a nitrogen containing heterocycle, a sulfur containing heterocycle, an oxygen containing heterocycle, a metal coordination group, a conjugate group, halogen, hydroxyl (OH), thiol (SH), keto (C=O), carboxyl (COOH), amide (CONR<sub>12</sub>), amidine (C(=NH)NR<sub>12</sub>R<sub>13</sub>), guanidine (NHC(=NH)NR<sub>12</sub>R<sub>13</sub>), glutamyl (R<sub>12</sub>OOCCH(NR<sub>12</sub>R<sub>13</sub>)(CH<sub>2</sub>)<sub>2</sub>C(=O)), nitrate (ONO<sub>2</sub>), nitro (NO<sub>2</sub>), nitrile (CN), trifluoromethyl (CF<sub>3</sub>), trifluoromethoxy (OCF<sub>3</sub>), O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, amino (NH<sub>2</sub>), azido (N<sub>3</sub>), hydrazino (NHNH<sub>2</sub>),

hydroxylamino ( $\text{ONH}_2$ ), sulfoxide ( $\text{SO}$ ), sulfone ( $\text{SO}_2$ ), sulfide ( $\text{S}$ -), disulfide ( $\text{S-S}$ ), silyl, a nucleosidic base, an amino acid side chain, a carbohydrate, a biopharmaceutically active moiety, or group capable of hydrogen bonding where the substituent groups are selected from hydroxyl, amino, alkoxy, alcohol, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, and alkynyl groups:

(h) optionally repeating steps (c) and (d) followed by step (g) to increase the length of the oligomeric compound bound to said solid support:

(i) treating said oligomeric compound bound to said solid support with acid to deprotect any protecting groups; and

(j) cleaving said oligomeric compound from said solid support.

46. (New) The process of claim 45 wherein said step (g) is conducted after said step (b).

47. (New) The process of claim 45 wherein said step (g) is conducted prior to step (d) for the addition of at least one monomeric subunit to said oligomeric compound.

48. (New) The process of claim 45 wherein said step (g) is conducted prior to each iteration of said step (d).

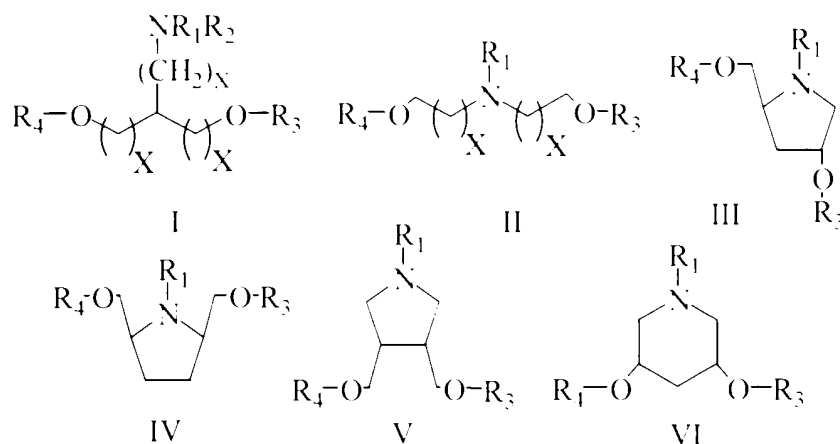
49. (New) The process of claim 45 wherein said step (g) is conducted only after at least one iteration of said step (e).

50. (New) The process of claim 45 wherein said step (g) is conducted after said step (f) for the addition of at least one monomeric subunit to said oligomeric compound.

52. (New) A method for preparing a combinatorial library comprising:



(a) selecting a plurality of aminodiol monomer subunits having the structure I, II, III, IV, V, or VI:



wherein:

each  $x$  is, independently, 0 to 5;

$R_1$  is a base labile amino protecting group;

$R_2$  is hydrogen or  $C_1$ - $C_{10}$  alkyl;

one of  $R_3$  or  $R_4$  is hydrogen or an activated phosphite group and the other of  $R_3$  or  $R_4$  is an acid labile hydroxyl protecting group;

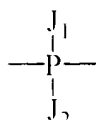
(b) attaching said aminodiol monomer subunits to a solid support to form a solid support bound aminodiol monomer subunits;

(c) treating said acid labile hydroxyl protecting groups with a dilute acid to form a free hydroxyl groups;

(d) reacting said free hydroxyl groups with further aminodiol monomer subunits having structure I, II, III, IV, V or VI thereby forming an oligomeric compound bound to said solid support, said oligomeric compound containing a phosphite linkage:

(e) optionally iteratively repeating steps (c) and (d) to increase the length of the oligomeric compound bound to said solid support:

(f) optionally, prior to step (c) or after step (d) oxidizing said phosphite linkage to form phosphate linking groups having formula:



wherein:

$J_1$  is =O or =S;

$J_2$  is OH or  $N(Y_0)T_0$ ;

$Y_0$  is H or  $(Q_2)_j-Z_2$ ;

$T_0$  is  $(Q_1)_k-Z_1$ , or together  $Y_0$  and  $T_0$  are joined in a nitrogen heterocycle;

$Q_1$  and  $Q_2$  independently are  $C_2$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{10}$  alkynyl,  $C_4$ -C-carbocyclo alkyl,  $C_4$ -C-carbocyclo alkenyl, a heterocycle, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, a polyalkyl glycol, or C- $C_{14}$  aralkyl;

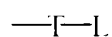
j and k independently are 0 or 1;

$Z_1$  and  $Z_2$  independently are H,  $C_1$ - $C_2$  alkyl,  $C_2$ - $C_{20}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl, C- $C_{15}$  aralkyl, halogen,  $CH=O$ ,  $OR_{12}$ ,  $SR_{12}$ ,  $NR_{12}R_{13}$ ,  $C(=NH)NR_{12}R_{13}$ ,  $CH(NR_{12}R_{13})$ ,  $NHC(=NH)NR_{12}R_{13}$ ,  $CH(NH_2)C(=O)OH$ ,  $C(=O)NR_{12}R_{13}$ ,  $C(=O)OR_{12}$ , a metal coordination group, a

reporter group, a nitrogen-containing heterocycle, a purine, a pyrimidine, a phosphate group, a polyether group, or a polyethylene glycol group.

provided that at least one of said aminodiol monomer subunits in each oligomeric compound of said library does not have structure III:

(g) prior to step (e) or after step (f) contacting said solid support bound aminodiol monomer subunits or said support bound oligomeric compounds with a base to remove said base labile amino protecting groups to form the solid support bound aminodiol monomer subunits or support bound oligomeric compounds having a free amine, and derivatizing said free amine with a group of the formula



wherein:

T is a single bond, a methylene group or a group having formula:



where:

$R_{10}$  is =O, =S, or =NR<sub>11</sub>;

$R_5$  and E, independently, are a single bond, CH=CH, C≡C, O, S, NR<sub>11</sub>, or C<sub>6</sub>-C<sub>14</sub> aryl;

each  $R_6$ ,  $R_7$ ,  $R_8$ ,  $R_9$ ,  $R_{11}$ ,  $R_{12}$  and  $R_{13}$  are, independently, H, alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, or aryl having 7 to about 14 carbon atoms;

m and n, independently, are 0 to 5;

p is 0 or 1;

q is 1 to about 10;

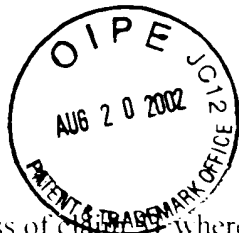
L is H, substituted or unsubstituted  $C_2-C_{10}$  alkyl, substituted or unsubstituted  $C_2-C_{10}$  alkenyl, substituted or unsubstituted  $C_2-C_{10}$  alkynyl, substituted or unsubstituted  $C_3-C_6$  carbocyclic alkyl, substituted or unsubstituted  $C_4-C_6$  carbocyclic alkenyl, substituted or unsubstituted  $C_4-C_6$  carbocyclic alkynyl, substituted or unsubstituted  $C_6-C_{14}$  aryl, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, a nitrogen containing heterocycle, a sulfur containing heterocycle, an oxygen containing heterocycle, a metal coordination group, a conjugate group, halogen, hydroxyl (OH), thiol (SH), keto (C=O), carboxyl (COOH), amide (CONR<sub>12</sub>), amidine (C(-NH)NR<sub>12</sub>R<sub>13</sub>), guanidine (NHC(=NH)NR<sub>12</sub>R<sub>13</sub>), glutamyl (R<sub>12</sub>OOCCH(NR<sub>12</sub>R<sub>13</sub>)(CH<sub>2</sub>)<sub>2</sub>C(=O)), nitrate (ONO<sub>2</sub>), nitro (NO<sub>2</sub>), nitrile (CN), trifluoromethyl (CF<sub>3</sub>), trifluoromethoxy (OCF<sub>3</sub>), O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, amino (NH<sub>2</sub>), azido (N<sub>3</sub>), hydrazino (NHNH<sub>2</sub>), hydroxylamino (ONH<sub>2</sub>), sulfoxide (SO), sulfone (SO<sub>2</sub>), sulfide (S-), disulfide (S-S), silyl, a nucleosidic base, an amino acid side chain, a carbohydrate, a biopharmaceutically active moiety, or group capable of hydrogen bonding where the substituent groups are selected from hydroxyl, amino, alkoxy, alcohol, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, and alkynyl groups:

(h) optionally repeating steps (c) and (d) followed by step (g) to increase the length of the oligomeric compounds bound to said solid support:

(i) treating said oligomeric compounds bound to said solid support with acid to deprotect any protecting groups; and

(j) cleaving said oligomeric compounds from said solid support.

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PATENT

52. (New) The process of claim 51 wherein said step (g) is conducted after said step (b).

53. (New) The process of claim 51 wherein said step (g) is conducted prior to step (e) for the addition of at least one monomeric subunit to each of said oligomeric compounds..

54. (New) The process of claim 51 wherein said step (g) is conducted prior to each iteration of said step (e).

55. (New) The process of claim 51 wherein said step (g) is conducted only after at least one iteration of said step (e).

56. (New) The process of claim 51 wherein said step (g) is conducted after said step (f) for the addition of at least one monomeric subunit to each of said oligomeric compounds. - -

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